General Recommendations on Immunization
Part One

Centers for Disease Control and Prevention
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General Recommendations on Immunization

Recommendations of the Advisory Committee on Immunization Practices (ACIP)

Continuing Education Examination available at http://www.cdc.gov/mmwr/cme/conted.html

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

General Recommendations on Immunization

- **An ACIP MMWR**
  - Timing and spacing
  - Contraindications and precautions
  - Preventing and managing adverse reactions to immunization
  - Vaccine administration
  - Storage and handling
  - Altered immunocompetence
  - Special situations
  - Vaccination records
  - Vaccination programs
  - Vaccine information sources

General Recommendations on Immunization

- **A chapter in the Pink Book**
  - Timing and spacing
  - Contraindications and precautions

Issues Regarding Timing and Spacing of Vaccines

- Interval between receipt of antibody-containing blood products and live vaccines
- Interval between doses of different vaccines not administered simultaneously
- Interval between subsequent doses of the same vaccine

Antibody-containing Blood Products

- Used to restore a needed component of blood or provide a passive immune response following disease exposure
- Sometimes circumstance dictate the use of antibody-containing blood products concurrently with a vaccine

Antibody and Live Vaccines

General Rule

- Inactivated vaccines are generally not affected by circulating antibody to the antigen
- Live, attenuated vaccines might be affected by circulating antibody to the antigen – an effectiveness concern

Antibody Products and Measles- and Varicella- containing Vaccines

Product given first	Action
Vaccine	Wait 2 weeks before giving antibody
Antibody	Wait at least 3 months before giving vaccine

Appendix A24: Interval Between Antibody-containing Products and Measles- and Varicella-containing Vaccines

Appendix A

Recommended intervals between administration of **immune globulin preparations** and **measles-** or **varicella-containing vaccine**

Product / Indication	Dose, including mg immunoglobulin G (IgG)/kg body weight	Recommended interval before measles or varicella-containing[1] vaccine administration
Blood transfusion		
- Red blood cells (RBCs), washed	10 mL/kg (negligible IgG/kg) IV	None
- RBCs, adenine-saline added	10 mL/kg (10 mg IgG/kg) IV	3 months
- Packed RBCs (hematocrit 65%)[2]	10 mL/kg (60 mg IgG/kg) IV	6 months
- Whole blood (hematocrit 35%-50%)[2]	10 mL/kg (80-100 mg IgG/kg) IV	6 months
- Plasma/platelet products	10 mL/kg (160 mg IgG/kg) IV	7 months
Botulinum Immune Globulin Intravenous (Human)	1.5 mL/kg (75 mg IgG/kg) IV	6 months
Cytomegalovirus IGIV	150 mg/kg maximum	6 months
Hepatitis A IG		
- Contact prophylaxis	0.02 mL/kg (3.3 mg IgG/kg) IM	3 months
- International travel	0.06 mL/kg (10 mg IgG/kg) IM	3 months
Hepatitis B IG (HBIG)	0.06 mL/kg (10 mg IgG/kg) IM	3 months
IGIV		
- Replacement therapy for immune deficiencies[3]	300-400 mg/kg IV	8 months
- Immune thrombocytopenic purpura treatment	400 mg/kg IV	8 months
- Measles IG, contact prophylaxis (immunocompromised contact)	400 mg/kg IV	8 months
- Postexposure varicella prophylaxis	400 mg/kg IV	8 months
- Immune thrombocytopenic purpura treatment	1,000 mg/kg IV	10 months
Measles IG, contact prophylaxis - Standard (i.e., nonimmunocompromised) contact	0.5 mL/kg (80 mg IgG/kg) IM	6 months
Monoclonal antibody to respiratory syncytial virus F protein (Synagis™)[4]	15 mg/kg (IM)	None
Rabies IG (RIG)	20 IU/kg (22 mg IgG/kg) IM	4 months
Tetanus IG (TIG)	250 units (10 mg IgG/kg) IM	3 months
Varicella IG[5]	125 units/10 kg (60-200 mg IgG/kg) IM, maximum 625 units	5 months

Spacing of Antibody-containing Products and MMR and Varicella Vaccines

Product	Interval
Washed red blood cells	0 months
Hepatitis A (IG)	3 months
Measles prophylaxis (IG) (normal contact)	6 months*
Plasma/platelet products	7 months
Intravenous immune globulin (IGIV)	7-11 months

*Immunocompromised contact 8 months

Products Containing Type-specific or Negligible Antibody

- **Palivizumab (Synagis)**
  - Contains only monoclonal RSV antibody
  - Does not interfere with live virus vaccination
- **Red blood cells (RBCs), washed**
  - Negligible antibody content

Exceptions to the General Rule

- **Antibody-vaccine spacing recommendations apply specifically to MMR and varicella-containing vaccines**
- **Does NOT apply to:**
  - Zoster vaccine (large amount of virus in the vaccine)
  - Yellow fever, oral typhoid (negligible antibody in the U.S. blood supply)
  - LAIV (viruses change annually)
  - Rotavirus (replication in GI tract)

Interval Between Doses of Different Vaccines

- Simultaneous administration
- Non-simultaneous administration

Simultaneous Administration

General Rule

- **All vaccines can be administered at the same visit as all other vaccines**
- **Exceptions:**
  - PCV13 and PPSV23: Give PCV13 first
  - MCV4-D (Menactra only) and PCV13 in asplenic children: Give PCV13 first

Non-simultaneous Administration: Live-vaccine Effectiveness

Combination	Minimum Interval
2 live injected or live intranasal influenza vaccine	4 weeks
All other	None

Spacing of Live Vaccines Not Given Simultaneously

- If 2 live parenteral or intranasal vaccines are given less than 28 days apart, the vaccine given 2nd should be repeated
- Antibody response from 1st vaccine interferes with replication of 2nd vaccine
- One exception: yellow fever vaccine and single-antigen measles vaccine

Interval Between Doses of the Same Vaccine

Intervals Between Doses

General Rule

- **Increasing** the interval between doses of a multidose vaccine does not diminish the effectiveness of the vaccine

Extended Interval Between Doses

- Not all permutations of all schedules for all vaccines have been studied
- Available studies of extended intervals have shown no significant difference in final titer
- It is not necessary to restart the series or add doses because of an extended interval between doses

Intervals Between Doses

General Rule

- Increasing the interval between doses of a multidose vaccine does not diminish the effectiveness of the vaccine

- Decreasing the interval between doses of a multidose vaccine may interfere with antibody response and protection

Recommended and Minimum Ages and Intervals Between Doses of Routinely Recommended Vaccines[1,2,3,4]

Vaccine and dose number	Recommended age for this dose	Minimum age for this dose	Recommended interval to next dose	Minimum interval to next dose
Diphtheria-tetanus-acellular pertussis (DTaP)-1[5]	2 months	6 weeks	8 weeks	4 weeks
DTaP-2	4 months	10 weeks	8 weeks	4 weeks
DTaP-3	6 months	14 weeks	6-12 months	6 months[6]
DTaP-4	15-18 months	15 months[7]	3 years	6 months
DTaP-5	4-6 years	4 years	—	—
Haemophilus influenzae type b (Hib)-1[5,8]	2 months	6 weeks	8 weeks	4 weeks
Hib-2	4 months	10 weeks	8 weeks	4 weeks
Hib-3[9]	6 months	14 weeks	6-9 months	8 weeks
Hib-4	12-15 months	12 months	—	—
Hepatitis A (HepA)-1	12-23 months	12 months	6-18 months	6 months
HepA-2	≥18 months	18 months	—	—
Hepatitis B (HepB)-1[5]	Birth	Birth	4 weeks-4 months	4 weeks
HepB-2	1-2 months	4 weeks	8 weeks-17 months	8 weeks
HepB-3[10]	6-18 months	24 weeks	—	—
Herpes zoster (HZV)[11]	≥60 years	60 years	—	—
Human papillomavirus (HPV)-1[12]	11-12 years	9 years	8 weeks	4 weeks
HPV-2	11-12 years (+ 2 months)	9 years (+ 4 weeks)	4 months	12 weeks[13]
HPV-3[13]	11-12 years (+ 6 months)	9 years (+24 weeks)	—	—
Influenza, inactivated (IIV)[14]	≥6 months	6 months[15]	4 weeks	4 weeks
Influenza, live attenuated (LAIV)[14]	2-49 years	2 years	4 weeks	4 weeks
Measles-mumps-rubella (MMR)-1[16]	12-15 months	12 months	3-5 years	4 weeks
MMR-2[16]	4-6 years	13 months	—	—
Meningococcal conjugate (MCV)-1[17]	11-12 years	6 weeks[18]	4-5 years	8 weeks
MCV-2	16 years	11 years (+ 8 weeks)	—	—
Meningococcal polysaccharide (MPSV4)-1[17]	—	2 years	5 years	5 years
MPSV4-2	—	7 years	—	—
Pneumococcal conjugate (PCV)-1[8]	2 months	6 weeks	8 weeks	4 weeks
PCV-2	4 months	10 weeks	8 weeks	4 weeks
PCV-3	6 months	14 weeks	6 months	8 weeks
PCV-4	12-15 months	12 months	—	—
Pneumococcal polysaccharide (PPSV)-1	—	2 years	5 years	5 years
PPSV-2[19]	—	7 years	—	—
Poliovirus, Inactivated (IPV)-1[6]	2 months	6 weeks	8 weeks	4 weeks
IPV-2	4 months	10 weeks	8 weeks-14 months	4 weeks
IPV-3	6-18 months	14 weeks	3-5 years	6 months
IPV-4[20]	4-6 years	4 years	—	—
Rotavirus (RV)-1[21]	2 months	6 weeks	8 weeks	4 weeks
RV-2	4 months	10 weeks	8 weeks	4 weeks
RV-3[22]	6 months	14 weeks	—	—
Tetanus-diphtheria (Td)	11-12 years	7 years	10 years	5 years
Tetanus-diphtheria-acellular pertussis (Tdap)[23]	≥11 years	7 years	—	—
Varicella (Var)-1[16]	12-15 months	12 months	3-5 years	12 weeks[24]
Var-2[18]	4-6 years	15 months[25]	—	—

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April, 2015

Included in Pink Book Appendix A-13

Appendix A

Recommended and Minimum Ages and Intervals Between Doses of Routinely Recommended Vaccines[1,2,3,4]				
Vaccine and dose number	**Recommended age for this dose**	**Minimum age for this dose**	**Recommended interval to next dose**	**Minimum interval to next dose**
Diphtheria-tetanus-acellular pertussis (DTaP)-1[5]	2 months	6 weeks	8 weeks	4 weeks
DTaP-2	4 months	10 weeks	8 weeks	4 weeks
DTaP-3	6 months	14 weeks	6-12 months	6 months[6]
DTaP-4	15-18 months	15 months[7]	3 years	6 months
DTaP-5	4-6 years	4 years	—	—
Haemophilus influenzae type b (Hib)-1[6,8]	2 months	6 weeks	8 weeks	4 weeks
Hib-2	4 months	10 weeks	8 weeks	4 weeks
Hib-3[9]	6 months	14 weeks	6-9 months	8 weeks
Hib-4	12-15 months	12 months	—	—
Hepatitis A (HepA)-1	12-23 months	12 months	6-18 months	6 months

Included in Pink Book Appendix A-13

Minimum Intervals and Ages

- Vaccine doses should not be administered at intervals less than the minimum intervals or earlier than the minimum age

When Can Minimum Intervals Be Used?

- Catch-up for a lapsed vaccination schedule
- Impending international travel
- NOT to be used routinely

The "Grace Period"

- ACIP recommends that vaccine doses given up to four days before the minimum interval or age be counted as valid
- Should not be used for scheduling future vaccination visits
- Use for reviewing vaccination records

MMWR 2011;60(RR-2)

Use of the "Grace Period"

- **Basic principles**
  - The recommended interval or age is preferred
  - The minimum interval can be used to catch up
  - The grace period is last resort

Use of the "Grace Period"

- To schedule a future appointment — **NO!**
- When evaluating a vaccination record — **Yes**
- Client is in the office or clinic early — **Maybe**

Use of the "Grace Period"

- **Client is in the office or clinic**
  - Client/parent is known and dependable — Reschedule
  - Client/parent is unknown or undependable — Vaccinate

Violations of Minimum Intervals and Minimum Ages

- Grace period may conflict with some state school entry requirements
- Immunization programs and/or school entry requirements may not accept some or all doses given earlier than the minimum age or interval, particularly varicella and/or MMR vaccines
- Providers should comply with local and/or state immunization requirements

Violations of Minimum Intervals and Minimum Ages

- **Minimum interval/age has been violated**
  - Dose invalid
- **The repeat dose should be administered at least a minimum interval from the invalid dose**

The "Pediarix Challenge"

- **Off-schedule administration could lead to 2 potential invalid doses:**
  - Hepatitis B birth dose (HepB1)
  - Pediarix at 2 months (HepB2)
  - Pediarix at 5 months (invalid HepB-age younger than 24 weeks)
  - Pediarix at 6 months (invalid HepB-interval since last dose less than 8 weeks)
- **CDC does NOT recommend a 5th dose of Hepatitis B vaccine in this situation**

Contraindications and Precautions

Vaccine Adverse Reaction

- **Adverse reaction**
  - Extraneous effect caused by vaccine
  - “Side effect"

Vaccine Adverse Reaction

- **Adverse reaction**
- **Adverse event**
  - Any medical event following vaccination
  - May be true adverse reaction
  - May be only coincidental

Vaccine Adverse Event Reporting System (VAERS)

- Reports from public and private sectors
- Providers should report any clinically significant adverse event that occurs after a vaccine, even if unsure whether or not the vaccine caused the event
- Providers may also report vaccine administration errors
- 1-800-822-7967 or online at www.vaers.hhs.gov

Types of Vaccine Adverse Reactions

- Local
- Systemic
- Allergic (least frequent)

Vaccine Adverse Reactions

- **Local**
  - Pain, swelling, redness at site of injection
  - Common with inactivated vaccines
  - Usually mild and self-limited

Vaccine Adverse Reactions

- **Local**
- **Systemic**
  - Fever, malaise, headache
  - Nonspecific
  - May be unrelated to vaccine

Live, Attenuated Vaccines

- Must replicate to produce immunity
- Symptoms usually mild
- Occur after an incubation period (usually 3-21 days)

Vaccine Adverse Reactions

- **Local**
- **Systemic**
- **Allergic**
  - Due to vaccine or vaccine component
  - Rare
  - Risk minimized by screening

Contraindication

- A condition in a recipient which greatly increases the chance of a serious adverse event

Precaution

- A condition in a recipient which may increase the chance or severity of an adverse event

OR

- May compromise the ability of the vaccine to produce immunity

Contraindications and Precautions

Permanent contraindications

- Severe allergic reaction to a prior dose of vaccine or to a vaccine component

Contraindications and Precautions

Permanent contraindications

- **Rotavirus vaccines only**
  - Severe Combined Immunodeficiency disease (SCID)
  - History of intussusception
- **Pertussis vaccines only**
  - Encephalopathy not due to another identifiable cause occurring within 7 days of pertussis vaccination

Contraindications and Precautions

Condition	Live	Inactivated
Allergy to component	C	C
Encephalopathy	---	C
Pregnancy	C	V*
Immunosuppression	C	V
Moderate/severe illness	P	P
Recent blood product	P**	V

C=contraindication
P=precaution
V=vaccinate if indicated
*Except HPV
**MMR and varicella-containing (except zoster vaccine and LAIV)

Appendix A

Guide to Contraindications and Precautions to Commonly Used Vaccines[1,*,†] (page 1 of 2)

Vaccine	Contraindications	Precautions
Hepatitis B (HepB)	• Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component	• Moderate or severe acute illness with or without fever • Infant weighing less than 2000 grams (4 lbs, 6.4 oz)[2]
Rotavirus (RV5 [RotaTeq], RV1 [Rotarix])	• Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component • Severe combined immunodeficiency (SCID) • History of intussusception	• Moderate or severe acute illness with or without fever • Altered immunocompetence other than SCID • Chronic gastrointestinal disease[3] • Spina bifida or bladder exstrophy[3]
Diphtheria, tetanus, pertussis (DTaP) **Tetanus, diphtheria, pertussis (Tdap)** **Tetanus, diphtheria (DT, Td)**	• Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component • For pertussis-containing vaccines: encephalopathy (e.g., coma, decreased level of consciousness, prolonged seizures) not attributable to another identifiable cause within 7 days of administration of a previous dose of DTP or DTaP (for DTaP); or of previous dose of DTP, DTaP, or Tdap (for Tdap)	• Moderate or severe acute illness with or without fever • Guillain-Barré syndrome (GBS) within 6 weeks after a previous dose of tetanus toxoid-containing vaccine • History of Arthus-type hypersensitivity reactions after a previous dose of tetanus or diphtheria toxoid-containing vaccine; defer vaccination until at least 10 years have elapsed since the last tetanus-toxoid containing vaccine • For pertussis-containing vaccines: progressive or unstable neurologic disorder (including infantile spasms for DTaP), uncontrolled seizures, or progressive encephalopathy until a treatment regimen has been established and the condition has stabilized **For DTaP only:** • Temperature of 105° F or higher (40.5° C or higher) within 48 hours after vaccination with a previous dose of DTP/DTaP • Collapse or shock-like state (i.e., hypotonic hyporesponsive episode) within 48 hours after receiving a previous dose of DTP/DTaP • Seizure within 3 days after receiving a previous dose of DTP/DTaP • Persistent, inconsolable crying lasting 3 or more hours within 48 hours after receiving a previous dose of DTP/DTaP
***Haemophilus influenzae* type b (Hib)**	• Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component • Age younger than 6 weeks	• Moderate or severe acute illness with or without fever
Inactivated poliovirus vaccine (IPV)	• Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component	• Moderate or severe acute illness with or without fever • Pregnancy
Pneumococcal (PCV13 or PPSV23)	• Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component (including, for PCV13, to any diphtheria toxoid-containing vaccine)	• Moderate or severe acute illness with or without fever
Measles, mumps, rubella (MMR)[4]	• Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component • Known severe immunodeficiency (e.g., from hematologic and solid tumors, receipt of chemotherapy, congenital immunodeficiency, or long-term immunosuppressive therapy[5] or patients with human immunodeficiency virus [HIV] infection who are severely immunocompromised)[6] • Pregnancy	• Moderate or severe acute illness with or without fever • Recent (within 11 months) receipt of antibody-containing blood product (specific interval depends on product)[7] • History of thrombocytopenia or thrombocytopenic purpura • Need for tuberculin skin testing[8]
Varicella (Var)[4]	• Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component • Known severe immunodeficiency (e.g., from hematologic and solid tumors, receipt of chemotherapy, congenital immunodeficiency, or long-term immunosuppressive therapy[5] or patients with HIV infection who are severely immunocompromised)[6] • Pregnancy	• Moderate or severe acute illness with or without fever • Recent (within 11 months) receipt of antibody-containing blood product (specific interval depends on product)[7] • Receipt of specific antivirals (i.e., acyclovir, famciclovir, or valacyclovir) 24 hours before vaccination; avoid use of these antiviral drugs for 14 days after vaccination.
Hepatitis A (HepA)	• Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component	• Moderate or severe acute illness with or without fever

(continued on page 2)

Technical content reviewed by the Centers for Disease Control and Prevention

IMMUNIZATION ACTION COALITION Saint Paul, Minnesota • 651-647-9009 • www.immunize.org • www.vaccineinformation.org

www.immunize.org/catg.d/p3072a.pdf • Item #P3072a (3/15)

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Included in Pink Book Appendix A-28-30

Vaccination During Pregnancy

- Live vaccines should not be administered to women known to be pregnant
- In general, inactivated vaccines may be administered to pregnant women for whom they are indicated
- HPV vaccine should be deferred during pregnancy

Vaccination During Pregnancy

- **Inactivated vaccines**
  - Routine
    - Influenza – any trimester
    - Tdap – 27 to 36 weeks
  - Vaccinate if indicated (HepA)
  - Vaccinate if indicated (HepB)
  - Vaccinate if increased risk (all others except HPV, PCV13, Hib)

Yellow Fever Vaccination in Pregnancy

- Live vaccines – do not administer (except yellow fever vaccine)
- No evidence of harm to fetus from yellow fever vaccination of mother, limited theoretical risk
- Pregnant women who must travel to areas where the risk for yellow fever is high should receive the vaccine

Vaccination of Immunosuppressed Persons

- Live vaccines should not be administered to severely immunosuppressed persons
- Persons with isolated B-cell deficiency may receive varicella vaccine
- Inactivated vaccines are safe to use in immunosuppressed persons, but the response to the vaccine may be decreased

Immunosuppression

- **Disease**
  - Congenital immunodeficiency
  - Leukemia or lymphoma
  - Generalized malignancy
- **Cancer Therapy**
  - Alkylating agents
  - Antimetabolites
  - Radiation

Immunosuppressive Drugs

- **Immune mediators**
- **Immune modulators**
- **Iso-antibodies (therapeutic monoclonal antibodies)**
  - Antitumor necrosis factor agents

Corticosteroids and Immunosuppression

- **The amount or duration of corticosteroid therapy needed to increase adverse event risk is not well-defined**

- **Dose generally believed to be a concern:**
  - 20 mg or more/day of prednisone for 2 weeks or longer
  - 2 mg/kg per day or more of prednisone for 2 weeks or longer

Corticosteroids and Immunosuppression(2)

- Does NOT apply to aerosols, topical, alternate-day, short courses (less than 2 weeks), physiologic replacement schedules
- Delay live vaccines for at least 1-3 month after discontinuation of high-dose therapy

Vaccination of Immunocompromised Persons

Safety:

- Immunocompromised persons are at increased risk of adverse events following live vaccines
- Live vaccines may be administered at least 3 months following termination of chemotherapy (at least 1 month after high-dose steroid use of 2 weeks or more)
- LAIV, MMR, varicella, and rotavirus vaccines may be administered to susceptible household and other close contacts

Vaccination of Immunocompromised Persons

- **Safety and efficacy**
- **Anti-tumor necrosis factor inhibitors**
  - Generally can treat like steroids
  - Some experts recommend waiting longer than one month after vaccination with live or inactivated vaccines
- **Other isoantibodies (e.g. lymphocyte depleting agents)**
  - Some experts recommend up to six months

Persons with HIV Infection

- Persons with HIV/AIDS are at increased risk for complications of measles, varicella, influenza and pneumococcal disease

Live, Attenuated Vaccines for Persons with HIV/AIDS*

Vaccine	Asymptomatic	Symptomatic*
Varicella	Yes	No
Zoster	No	No
MMR	Yes	No
MMRV	No	No
LAIV	No	No
Rotavirus	Consider	Consider
Yellow Fever	Consider	No

Yes=vaccinate No=do not vaccinate

*See specific ACIP recommendations for details.

Vaccination of Hematopoietic Cell Transplant (HCT) Recipients

- Antibody titers to VPDs decline during the 1-4 years after allogeneic or autologous HCT if the recipient is not revaccinated
- HCT recipients are at increased risk of some VPDs, particularly due to encapsulated bacteria
- Revaccination recommended beginning 6-24 months post-transplant

MMWR 2000;49(RR-10)

Vaccination of HCT Recipients

- Inactivated influenza vaccine at least 4-6 months following transplant and annually thereafter

- Inactivated vaccines (DTaP, Td, IPV, PCV13, PPSV23, Hepatitis B, Hib, HPV, MCV4) at 6 months

- MMR, varicella, yellow fever vaccines at 24 months if immunocompetent

Rubin, LG, Levin MJ, Ljungman P., et. Al. 2013 IDSA Clinical Practice Guidelines for Vaccination of the Immunocompromised Host. Clin. Infect. Dis. 2014; 58: e-44-100.